Remarks

I. Support for Amendments

Support for the foregoing amendments to the claims may be found throughout the specification as originally filed, either inherently or explicitly. Specifically, support for the amendments to claim 52 may be found in the specification at page 10, line 18-27 and Example 9, pages 82-87; and support for the amendment to claim 65 maybe found in the specification at Example 9, pages 82-87. Hence, the foregoing amendments to the claims do not add new matter, and their entry and consideration are respectfully requested.

II. Status of the Claims

By the foregoing amendments, claim 1 has been cancelled, and claims 52 and 65 have been amended. These amendments do not add new matter. Upon entry of the foregoing amendments, claims 52-67 are pending in the application, with claim 52 being the sole independent claim.

III. Summary of the Office Action

In the Office Action dated March 26, 2002, the Examiner has objected to the drawings and has made two rejections of the claims. Applicants respectfully offer the following remarks to overcome or traverse each of these elements of the Office Action.

IV. The Objection to the Drawings is Accommodated

In the Office Action at page 2, section 1, the Examiner has objected to the drawings and has required the submission of formal drawings. As noted above, formal drawings for the present application are filed concurrently herewith. Accordingly, this objection has been fully accommodated; reconsideration and withdrawal are respectfully requested.

V. The Rejection Under 35 U.S.C. § 112 Second Paragraph

In the Office Action at pages 2-5, sections 2-11, the Examiner has rejected claims 1 and 52-67 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection, in view of the following remarks.

A. The Recitation of "In vivo" and "In vitro"

The Examiner has first rejected claims 1 and 52-67 for alleged indefiniteness for reciting "*in vivo*" or "*in vitro*." *See* Office Action at page 2, section 4.

By the foregoing amendments, and for reasons unrelated to this rejection, claim 1 has been cancelled thus rendering moot the portion of this rejection that may have applied to that claim. Applicants respectfully traverse this rejection as it may be applied to the remaining claims.

The Examiner first contends that claims 52-67 are indefinite for allegedly reciting "*in vivo*" or "*in vitro*," which the Examiner asserts is not defined in the present specification. *See* Office Action at page 2, section 4. Applicants respectfully disagree.

Claim 52, and the remaining claims depending therefrom, do not recite "*in vivo*." Moreover, contrary to the Examiner's contentions, the term "*in vitro*" is sufficiently defined in the specification. For example, Figures 2A, 3A and 4A, as well as the description of these figures in the specifications at pages 17-19, clearly indicate that an "*in vitro*" recombination reaction, as that term is used in the present application, takes place outside of host cells. This conclusion is also supported by the text of Example 1 (particularly at page 52, lines 17-23, and at page 53, line 32 to page 54, line 21); Examples 2 (particularly at page 55, line 37 to page 56, line 7); Example 3 (particularly at page 59, line 13-21, and at page 60, line 30-40); Example 4 (particularly at page 62, lines 22-30); and throughout the remaining Examples. This meaning for *in vitro* comports with the standard definition for this term, which is "outside the living body and in an artificial environment." *Webster's Ninth New Collegiate Dictionary*, Springfield, MA: Merriam-Webster Inc., p. 637 (1987) (copy attached hereto for the Examiner's convenience). Finally, that the term "*in vitro*" is used throughout the specification as an alternative to "*in vivo*" (*i.e.*, "*in vitro* or *in vivo*;" *see*, *e.g.*, Specification at page 1, lines 21-22; at page 6, line 23; at page 21, line 3; at page 31, line 9; etc.) indicates that *in vitro* recombination is distinguished from *in vivo* recombination which takes place in host cells. Thus, in view of the clear guidance provided by the present specification, one of ordinary skill would readily understand that "*in vitro* recombination," as that phrase is used in the present claims, means a recombination reaction that takes place outside of a host cell.

As the Board had held:

> [35 U.S.C. §112 second paragraph] merely requires that the claims set forth and circumscribe a particular area with a reasonable degree of precision and particularity. The definiteness of the claim language employed must not be

> analyzed in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one having ordinary skill in the pertinent art.

Ex parte Moelands, 3 USPQ2d 1474, 1476 (Bd. Pat. App. Int. 1987) (citing *In re Moore*, 439 F.2d 1232 (CCPA 1971). As noted above, one of ordinary skill would readily understand the meaning of "*in vitro*," as that term is used in claims 52-67. Hence, these claims comport with the requirements of 35 U.S.C. §112, second paragraph, as interpreted under *Moelands* and *Moore*. Thus, this portion of the rejection is in error; reconsideration and withdrawal therefore are respectfully requested.

B. The Recitation of "Product Molecules"

The Examiner has next rejected claim 1 for allegedly being indefinite due to the recitation of "product molecules." *See* Office Action at page 3, section 5. By the foregoing amendments, claim 1 has been cancelled for reasons unrelated to this rejection. Thus, this portion of the rejection has been rendered moot.

C. The Recitation of "Vector Donor"

The Examiner has next rejected claim 1 for allegedly being indefinite for reciting "vector donor." *See* Office Action at page 3, section 6. By the foregoing amendments, claim 1 has been cancelled for reasons unrelated to this rejection. Thus, this portion of the rejection has been rendered moot.

D. The Omission of Essential Steps

The Examiner has next rejected claim 1 for being incomplete for allegedly omitting essential steps. *See* Office Action at page 4, section 8. Applicants respectfully disagree with the Examiner, and assert that claim 1 does not omit essential steps. Nevertheless, by the foregoing amendments, claim 1 has been cancelled for reasons unrelated to this rejection. Thus, this portion of the rejection has been rendered moot.

E. The Recitation of the Trademark/Trade Name "PCR"

The Examiner has next rejected claim 52 as being indefinite for reciting the trademark/trade name "PCR," which the Examiner contends makes the scope of the claim uncertain. *See* Office Action at page 4, section 9. By the foregoing amendments, claim 52 has been amended to identify/describe "PCR" as "Polymerase Chain Reaction," as suggested by the Examiner in the Office Action at page 4, section 9. Hence this portion of the rejection has been accommodated; reconsideration and withdrawal therefore are respectfully requested.

F. The Recitation of "Mutants Thereof"

The Examiner next contends that claims 60, 62 and 64 are indefinite for reciting"mutants thereof." *See* Office Action at pages 4-5, section 10. Applicants respectfully traverse this portion of the rejection.

In making this rejection, the Examiner contends that:

> [o]ne of ordinary skill in the art would not know how to interpret the metes and bounds of this limitation. A mutation of a recombination site may be closely patterned after the subject recombination site or may be very loosely patterned after the subject recombination site, such that it may bear no

> resemblance or form recognizable as the subject recombination site which maybe chemically and/or biologically totally unrelated in function or form to the subject recombination site.

Office Action at page 4, section 10, line 1, to page 5, line 2. Applicants respectfully disagree with these contentions.

Claims 60, 62 and 64 all depend from independent claim 52, which requires that the recombination sites (or mutants thereof) used be functional in recombinational cloning reactions (by reciting the combining of nucleic acid molecules "under conditions such that recombination occurs between said first and third and said second and fourth recombination sites . . ."). Hence, the "mutants" of a given recombination site recited in claims 60, 62 and 64 would be *biologically* related to the subject recombination site in that the mutants would still have to be functional in recombinational cloning reactions. Moreover, the present specification provides detailed teachings of how to prepare functional mutant recombination sites (*see*, *e.g.*, specification at pages 41-44, and throughout the Examples), and discloses a substantial number of non-limiting examples of mutants of recombination sites (including nucleotide sequences thereof; *see*, *e.g.*, specification at pages 44-46). Hence, the "mutants" of a given recombination site recited in claims 60, 62 and 64 are also *chemically* related to the subject recombination site, since the structures of the mutants are based on the structures of the non-mutant recombination site.

Accordingly, Applicants respectfully assert that one of ordinary skill could readily determine the metes and bounds of the term "mutants thereof" as used in claims 60, 62 and 64, based on the guidance provided by the present specification. Hence, claims 60, 62 and 64 comport with the requirements of 35 U.S.C. §112, second paragraph, as interpreted under

Moelands and *Moore*. Thus, this portion of the rejection is in error; reconsideration and withdrawal therefore are respectfully requested.

G. The Recitation of "Said Product Nucleic Acid Molecule"

The Examiner next contends that claim 65 is indefinite for reciting "said product nucleic acid molecule," for which the Examiner contends there is insufficient antecedent basis. *See* Office Action at page 5, section 11. By the foregoing amendments, claim 65 has been amended to replace the phrase "product nucleic acid molecule," with the phrase "PCR product." Since claim 52, from which claim 65 depends, also recites "a PCR product," the recitation of "said PCR product" in claim 65 has antecedent basis in claim 52. Hence, this portion of the rejection has been accommodated; reconsideration and withdrawal are respectfully requested.

H. Summary

In view of the foregoing remarks, Applicants respectfully assert that claims 52, 60, 62, 64 and 65 as currently presented particularly point out and distinctly claim the subject matter regarded by Applicants as the invention. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph, therefore are respectfully requested.

VI. The Rejection of Claim 1 Under 35 U.S.C. § 102(e) Over Elledge Is Rendered Moot

The Examiner has first rejected claim 1 for allegedly being anticipated by Elledge (U.S. Patent No. 5,851,808: Doc. AB3, of record; hereinafter "Elledge"). *See* Office Action at page 5, section 4. By the foregoing amendments, and for reasons unrelated to this rejection, claim 1 has been cancelled. Thus, this rejection has been rendered moot.

VII. The Rejection Under 35 U.S.C. § 102(e) Over Elledge Is Traversed

In the Office Action at pages 6-7, section 14, the Examiner has rejected claims 52-57 under 35 U.S.C. § 102(e) as being anticipated by Elledge. Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contends that:

> [Elledge] taught an in vitro method of cloning a polymerase chain reaction product comprising obtaining a polymerase chain reaction product comprising a first recombination site and a second recombination site which do not recombine with each other and combining the polymerase chain reaction product with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other under conditions such that recombination occurs between the first and third recombination sites and the second and fourth recombination sites thereby making a product vector.

Office Action at page 6, section 14, line 2, to line 9. Applicants respectfully disagree with these contentions.

Contrary to the Examiner's above-noted contentions, Elledge does not disclose all of the elements of independent claim 52 (and thus of the remaining claims that ultimately depend from claim 52). In particular, Elledge does not disclose an operative method comprising

combining *in vitro*, a PCR product comprising two recombination sites which do not recombine with each other, with a vector comprising two recombination sites which do not recombine with each other, thereby producing a product vector. Instead, Elledge only discloses a method for combining *in vitro* a pUNI vector construct having a single recombination site with a pHOST expression vector also having a single recombination site. *See* Elledge at col. 23, line 31 to col. 24, line 25, and in Figures 8A and 9A. Moreover, at least one additional element of the claimed invention is missing from Elledge: performance of the recombination reaction *in vitro* between a PCR product and a vector, each bearing at least two recombination sites that do not recombine with each other. In the sections referred to by the Examiner in making this rejection, Elledge discloses recombination reactions that take place *in vivo* - - *i.e.*, inside of a host cell. *See* Elledge at col. 29, lines 10-51. Indeed, without the use of the host cell which provides the recombination protein that drives the reaction (in this case, Cre which catalyzes recombination between two *lox* sites), the methods disclosed in this portion of Elledge relied upon by the Examiner would not work to recombine the PCR product and the vector. Hence, Elledge does not disclose an *in vitro* recombination reaction between a PCR product and a vector, each having at least two recombination sites that do not recombine with each other.

Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). As noted above, Elledge does not expressly or inherently disclose an *in vitro* recombination method using PCR products and vectors, each having two recombination sites that do not

recombine with each other. Hence, under *Kalman*, this reference cannot and does not anticipate the claims as currently presented.

In view of the foregoing remarks, Applicants respectfully assert that Elledge cannot and does not anticipate the claims as currently presented. Reconsideration and withdrawal of the rejection of claims 52-57 under 35 U.S.C. § 102(e) over Elledge therefore are respectfully requested.

VII. Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider and withdraw all of the outstanding rejections.

It is believed that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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Version with markings to show changes made

In the Claims:

(a) Claim 1 has been cancelled without prejudice or disclaimer.

(b) Pending claims 52 and 65 are sought to be amended as follows:

52. (Once amended) An *in vitro* method of cloning a [PCR] Polymerase Chain Reaction (PCR) product comprising:

(a) obtaining a PCR product comprising a first recombination site and a second recombination site which do not recombine with other; and

(b) combining said PCR product *in vitro* with a vector comprising a third recombination site and a fourth recombination site which do not recombine with each other, under conditions such that recombination occurs between said first and third and said second and fourth recombination sites, thereby producing a vector product.

65. (Once amended) The method of claim 52, wherein said PCR product [nucleic acid molecule] and said vector are combined in the presence of at least one recombination protein.